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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,233	10/24/2003	Zehra Kaymakcalan	BBC-193	1420

959 7590 10/21/2005

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EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,233	KAYMAKCALAN ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/18/05, 8/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment/remarks, filed 08/08/2005, are acknowledged.

Claims 5-8, 12-14, 17-22, 25-27, 30, and 31 have been amended.
Claims 32 – 49 have been added.
Claims 1 – 49 are pending.

Claims 1 – 49, as they read on the elected Invention of a method for treating rheumatoid arthritis by administering anti-TNFα antibodies, are under consideration in the instant application.

2. This Office Action will be in response to applicant's arguments, filed 08/08/2005.

The rejections of record can be found in the previous Office Action, mailed 02/07/2005.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

3. The objections and rejections of record have been withdrawn in view of Applicant's amendment and arguments, except as set forth supra.

4. Applicant's IDS documents, filed 01/18/2005 and 08/08/2005, are acknowledged, and have been considered.

Applicant states that copies of foreign patent documents and non-patent literature (Refs. No. A8-A18 and B14-D4 on IDS filed 01/18/2005) have been enclosed. However, references C1 – D4 have not been located in the file of the instant application, and have been lined through. Applicant is invited to resubmit these references to complete the record. The Examiner apologizes for the inconvenience to Applicant.

Reference E4 on IDS filed 08/08/2005 has been considered, but lined through as it is not appropriate for printing on the face of a Patent.

5. Applicant's submission of substitute specification is acknowledged.

6. Claims 1 – 6, 8 – 13, 15 – 19, 21 – 26, and 28 – 31 stand rejected, and newly added claims 32 – 37, 40 – 45, and 49 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 – 6, 8 – 13, 15 – 19, 21 – 26, and 28 – 37, 40 – 45, and 49 are indefinite in the recitation of a "low dose" therapy, because the metes and bounds of the claimed invention are unclear, so that one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that based on the plain language of the claims and the teachings of in the specification, the claims are clear and definite, because the specification teaches that the phrase "low dose" means an amount of a TNFα inhibitor which is substantially lower than that ordinarily employed.

This is not found persuasive, because first, "substantially lower" is still a relative term, and the specification lacks some standard for measuring the degree intended; and second, the "amount ordinarily employed" is itself not adequately defined.

Applicant further argues that the specification provides working examples which describe exemplary dosage amounts of a low dose treatment.

This is not found persuasive, because the exemplary dosage amounts do not limit the claim language as instantly recited.

Applicant further argues that one of ordinary skill in the art could easily determine the dose of the specific TNFα inhibitor ordinarily given to a subject.

This is not found persuasive, because there in no single dose of TNFα inhibitor "ordinarily" given to a subject. For example, Schentrup (PharmaNote, 2003, 18(10): 1 – 8) teaches administration of anti-TNFα antibody adalimumab (D2E7) in doses of 20 mg, 40 mg, and 80 mg. Therefore, it is unclear to a skilled artisan which dose regiment to use as a reference point to arrive at the "low dose" instantly claimed. Furthermore, since the instant claims and specification exemplify the doses expressed in mg/kg, and the art teaches absolute doses, such as 20 or 80 mg, the "ordinary" dose expressed in mg/kg will vary depending on the subject's body weight. In view of the above, the specification does not sufficiently define the metes and bounds of the claimed invention.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

7. Claims 1 – 4, 8 – 11, 15 – 17, 21 – 24, 28 – 29, and 31 stand rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a TNFα inhibitor which is an anti-TNFα antibody, does not reasonably provide enablement for the full breadth of the genus of "TNFα inhibitors."

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that one of ordinary skilled in the art would recognize based on the teachings in the specification and the knowledge In the art at the time of filing that any compound which inhibits TNFα may be used in a low dosage therapy of the invention.

This is not found persuasive, at least because the instant claims include in their breadth any TNFα inhibitors, including those which are currently not known in the art and for which no "ordinary" dosage has been established. Therefore, it is unpredictable whether a dose which is "substantially lower" than one that may be determined to be "ordinary" will also be effective.

Applicant further argues that the specification discloses "numerous" examples of TNFα inhibitors to support a genus of inhibitors.

This is not found persuasive, because although the specification discloses three examples of TNFα inhibitors, namely D2E7, Remicade and Enbrel, they are disclosed to differ markedly in their effect on the microscopic signs of disease in a mouse model of rheumatoid arthritis at a dose of e.g. 0.1 mg/kg (e.g. pages 29 – 30). In view of this variability, it remains unpredictable how effective other inhibitors of TNFα will be in alleviating microscopic or other symptoms of the disease, in model systems or in disease subjects.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

8. Claims 1 – 4, 8 – 11, 15 – 17, 21 – 24, 28 – 29, and 31 stand rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

Applicant is not in possession of a method for treating a disorder by administering a "TNFα inhibitor," as generically recited in the instant claims.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant arguments have been addressed in section 7 supra.

The rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

9. Claims 1 – 31 stand rejected, and newly added claims 32 – 49 are rejected, under **35 U.S.C. 102(b)** as being anticipated by Salfeld et al. (US Patent No. 6,258,562; see entire document).

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that Salfeld et al. do not teach or suggest administering a *low dose* of a TNFα inhibitor, i.e. a dose which is less than that ordinarily used for treatment.

This is not found persuasive, because the dose range taught by Salfed et al. (0.1 – 20 mg/kg) overlaps with the dose range instantly claimed (0.01 – 1.0 mg/kg).

It is noted that the functional properties of the anti-TNFα antibody (e.g. as recited in claim 41) are intrinsic properties of antibody D2E7 taught by Salfeld et al. It is further noted that treatment of specific symptoms or rheumatoid arthritis (e.g. as recited in claim 43) is intrinsic in treatment of rheumatoid arthritis as taught by Salfeld et al.

Therefore the rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

10. Claims 1 – 31 stand rejected, and newly added claims 32 – 49 are rejected, under **35 U.S.C. 102(e)** as being anticipated by Salfeld et al. (US Patent No. 6,509,015; see entire document).

Applicant's arguments have been fully considered but have not been found convincing.

Applicant arguments have been addressed in section 9 supra.

It is noted that Salfeld et al. disclose at least at column 23, lines 27 – 31 that the range of therapeutically effective amount of the antibody of the invention is 0.1 – 20 mg/kg, a range overlapping with the one instantly claimed (0.01 – 1.0 mg/kg).

The rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

11. Claims 1 – 31 stand rejected, and newly added claims 32 – 49 are rejected, under the judicially created doctrine of **obviousness-type double patenting** as being unpatentable over claims 1 – 100 of U.S. Patent No. 6,509,015. Although the conflicting claims are not identical, they are not patentably distinct from each other for reasons set forth in the prior Office Action.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant arguments are essentially the same as those set forth in response to the rejection under 35 U.S.C. 102(e), and have been addressed in section 10 supra.

It is noted that the claims of the '015 Patent are interpreted in light of the specification, and as such, encompass the anti-TNFα antibody dosage range of 0.1 – 20 mg/kg. Therefore, the claims of the '015 Patent anticipate the instant claims directed to administering a "low dose" of TNFα inhibitor, because the "low dose" encompasses at least the range of 0.01 – 1.0 mg/kg, as recited e.g. in claim 38.

The rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

12. Conclusion: no claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
10/7/05

October 14, 2005